```
=> fil reg; d stat que l5
FILE 'REGISTRY' ENTERED AT 09:38:18 ON 27 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   25 JUN 2003  HIGHEST RN 537653-06-8
DICTIONARY FILE UPDATES:  25 JUN 2003  HIGHEST RN 537653-06-8

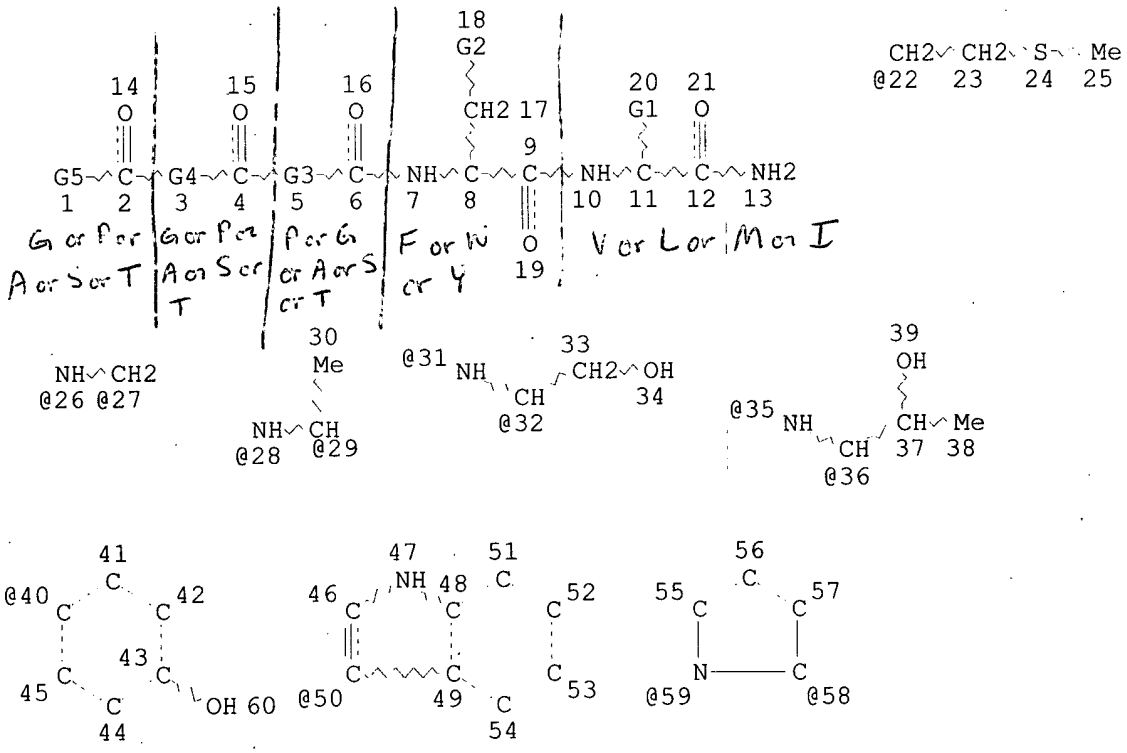
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf
```

L3 STR

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VAR G2=PH/40/50
VAR G3=59-4 58-6/26-4 27-6/31-4 32-6/35-4 36-6/28-4 29-6
VAR G4=59-2 58-4/26-2 27-4/31-2 32-4/35-2 36-4/28-2 29-4
VAR G5=58/27/29/32/36
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 60

STEREO ATTRIBUTES: NONE
L5 19 SEA FILE=REGISTRY SSS FUL L3

100.0% PROCESSED 366006 ITERATIONS 19 ANSWERS
SEARCH TIME: 00.00.05

=> d sqide 15

L5 ANSWER 1 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 497221-38-2 REGISTRY – Retrieves CAPI citation # 2
CN L-Valinamide, L-alanylglycyl-L-tyrosyl-L-lysyl-L-prolyl-L-.alpha.-aspartyl-L-.alpha.-glutamylglycyl-L-lysyl-L-arginylglycyl-L-.alpha.-aspartyl-L-alanyl-L-cysteinyl-L-.alpha.-glutamylglycyl-L-.alpha.-aspartyl-L-serylglycylglycyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 23 = sequence length
NTE modified

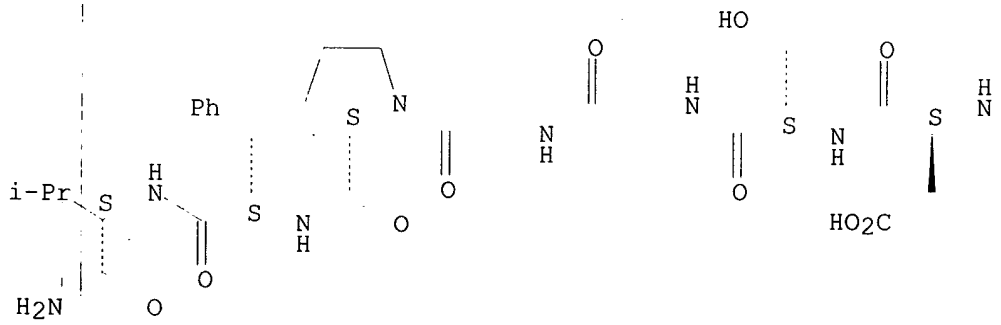
type	------ location ------		description
terminal mod.	Val-23	-	C-terminal amide

SEQ 1 AGYKPDEGKR GDACEGDSGG PFV

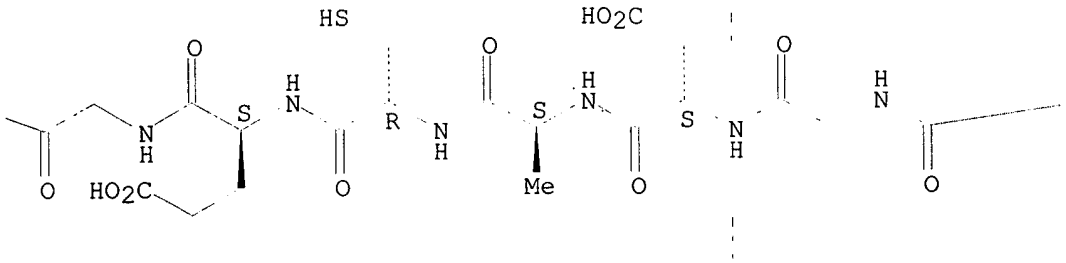
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C97 H147 N29 O35 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

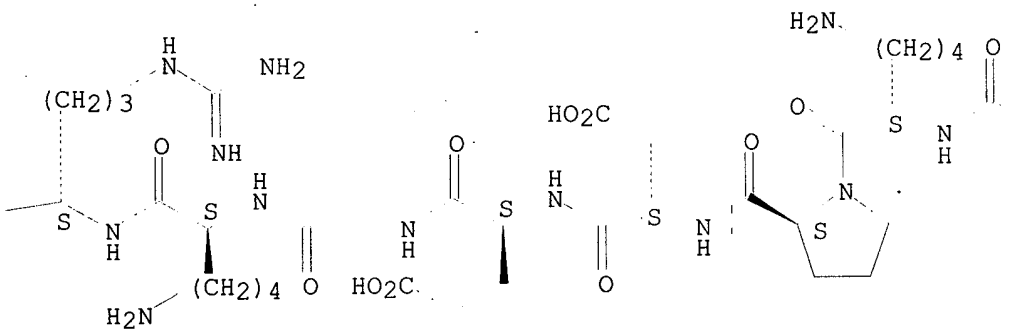
PAGE 1-A



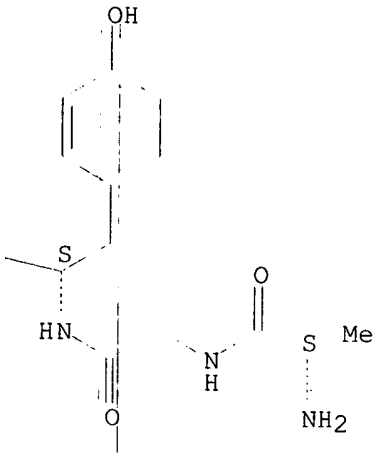
PAGE 1-B



PAGE 1-C



PAGE 1-D



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

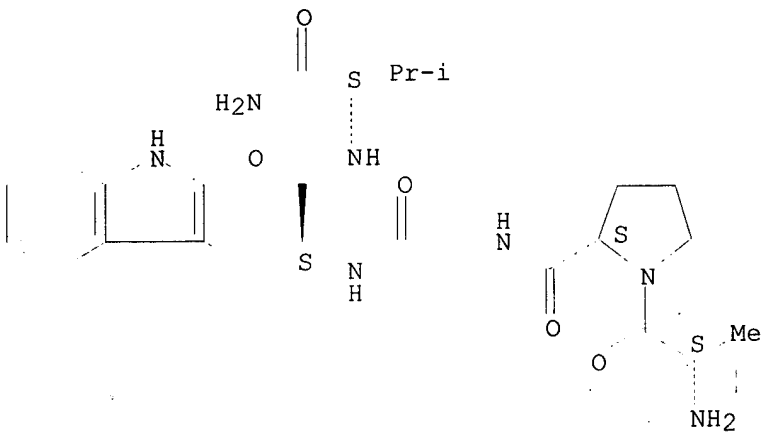
=> d sqide l5 2-19

L5 ANSWER 2 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 314057-76-6 REGISTRY - Matrix CAPL record #3
CN L-Valinamide, L-alanyl-L-prolylglycyl-L-tryptophyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 5
NTE modified

type	------ location ------		description
terminal mod.	Val-5	-	C-terminal amide

SEQ 1 APGWV
MF C26 H37 N7 O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



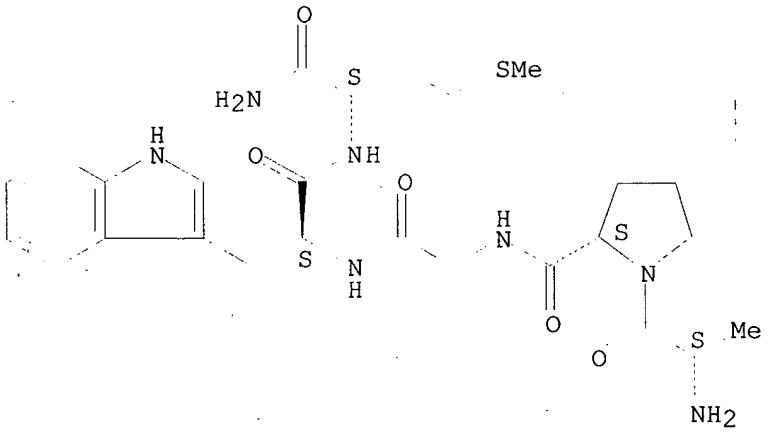
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 3 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 314057-69-7 REGISTRY Matches CAPL record #3
CN L-Methioninamide, L-alanyl-L-prolylglycyl-L-tryptophyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 5
NTE modified

type	------ location ------		description
terminal mod.	Met-5	-	C-terminal amide

SEQ 1 APGWM
MF C26 H37 N7 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



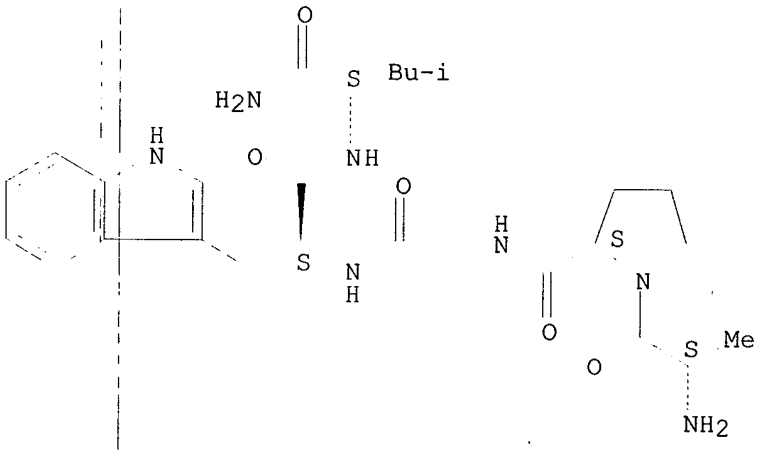
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 4 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 314057-67-5 REGISTRY matches CAPL record # 3
CN L-Leucinamide, L-alanyl-L-prolylglycyl-L-tryptophyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 5
NTE modified

type	------ location ------		description
terminal mod.	Leu-5	-	C-terminal amide

SEQ 1 APGWL
MF C27 H39 N7 O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



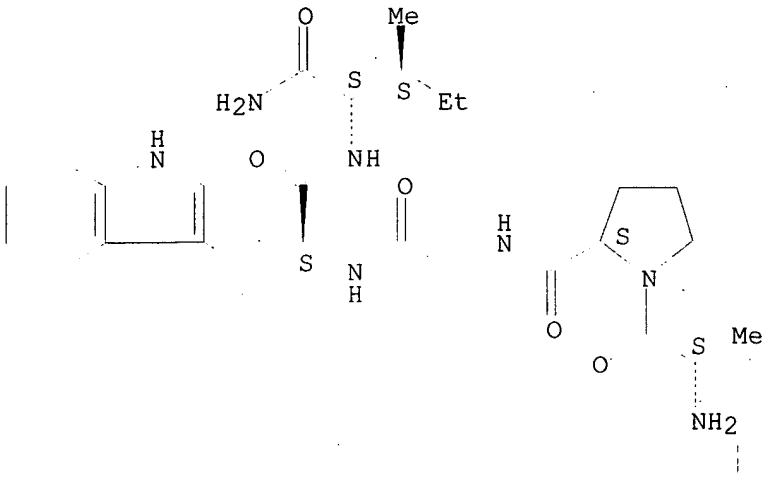
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 5 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 314057-66-4 REGISTRY matches CAPL record # 3
CN L-Isoleucinamide, L-alanyl-L-prolylglycyl-L-tryptophyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 5
NTE modified

type	------ location ------		description
terminal mod.	Ile-5	-	C-terminal amide

SEQ 1 APGWI
MF C27 H39 N7 O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 6 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 208921-17-9 REGISTRY matches CAPL record #4
CN L-Valinamide, N-acetyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-glutamyl-L-valyl-L-valyl-L-threonyl-L-seryl-L-threonyl-L-tryptophyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

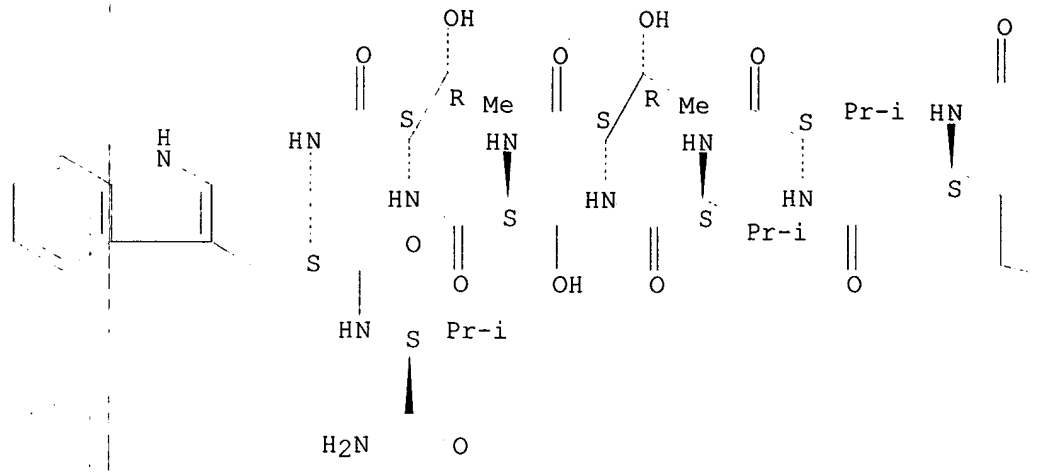
type	location		description
terminal mod.	Asp-1	-	N-acetyl
terminal mod.	Val-10	-	C-terminal amide

SEQ 1 DLEVVTSTWV

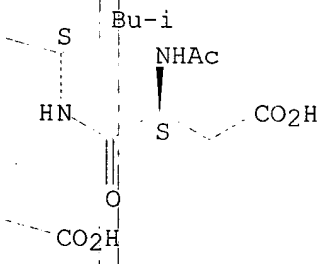
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C54 H84 N12 O18
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

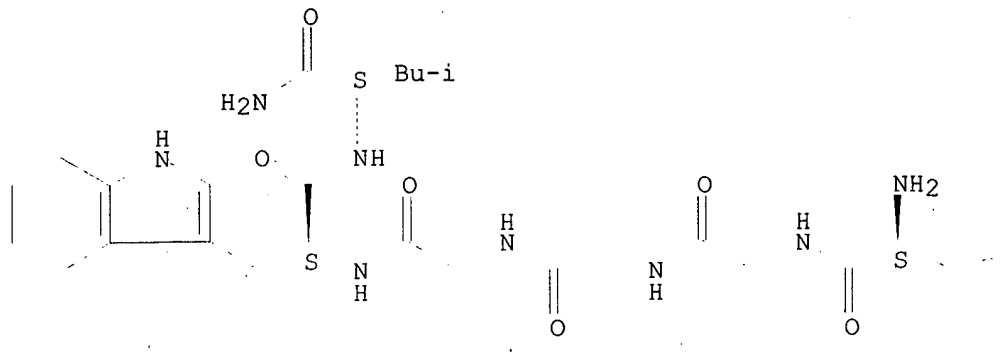
L5 ANSWER 7 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 197917-26-3 REGISTRY matches CAPL record #5
CN L-Leucinamide, L-tyrosylglycylglycylglycyl-L-tryptophyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 6
NTE modified

type	------ location ------		description
terminal mod.	Leu-6	-	C-terminal amide

SEQ 1 YGGGWL
MF C32 H42 N8 O7
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

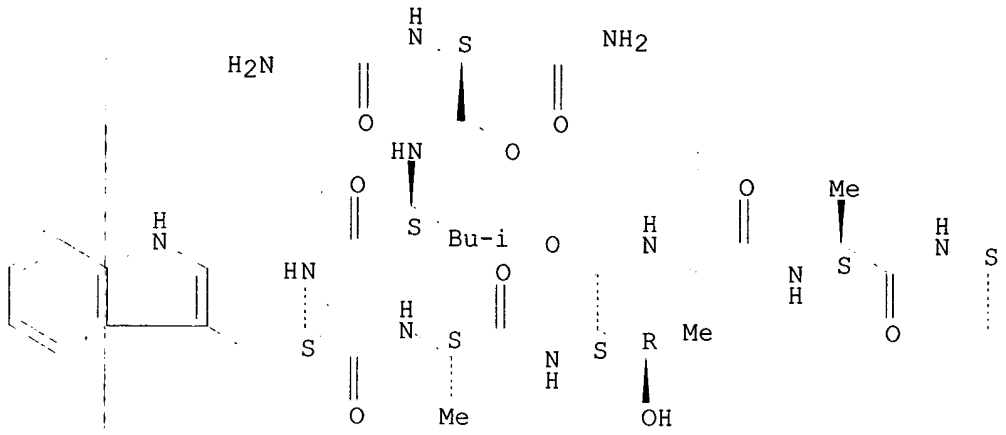
L5 ANSWER 8 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 184770-60-3 REGISTRY matches CAPL record #6
CN Neuromedin B (swine spinal cord), 8-L-alanine- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Neuromedin B (pig spinal cord), 8-L-alanine-
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

type	------ location ------		description
terminal mod.	Met-10	-	C-terminal amide

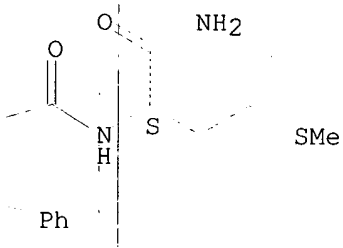
SEQ 1 GNLWATGAFM
MF C49 H71 N13 O12 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

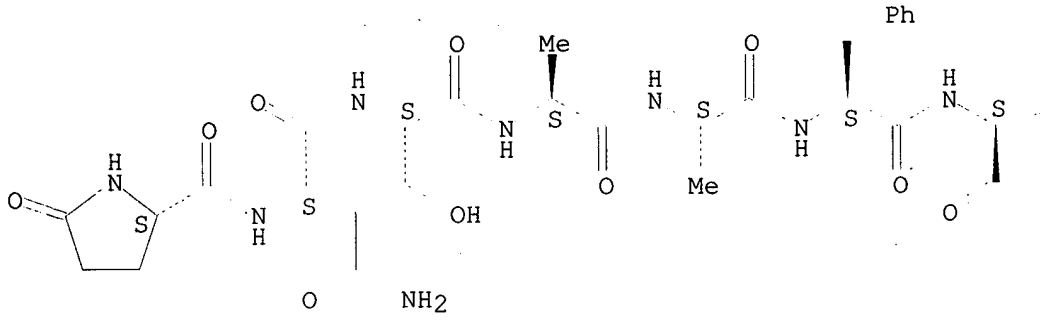
L5 ANSWER 9 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 152868-80-9 REGISTRY Matches CAPE word #8
CN L-Valinamide, 5-oxo-L-prolyl-L-asparaginyl-L-seryl-L-alanyl-L-alanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 7
NTE modified

type	------ location ------		description
terminal mod.	Val-7	-	C-terminal amide
uncommon	Glp-1	-	-

SEQ 1 XNSAAFV
MF C32 H47 N9 O10
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

Pr-i

NH2

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

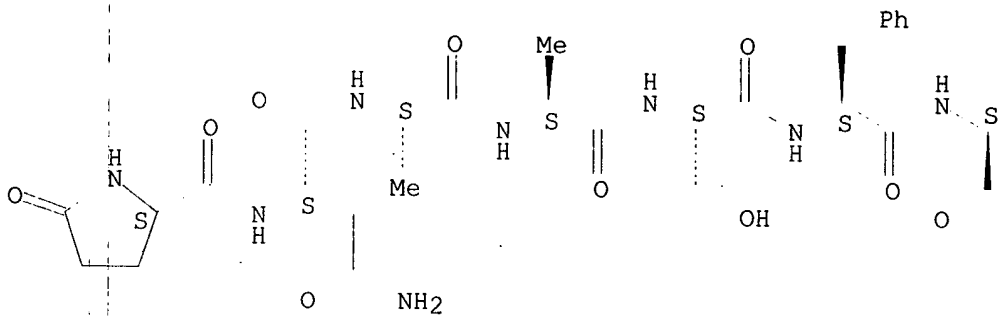
L5 ANSWER 10 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 152868-78-5 REGISTRY Matarus CAR record #8
CN L-Valinamide, 5-oxo-L-prolyl-L-asparaginyl-L-alanyl-L-alanyl-L-seryl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 7
NTE modified

type	------ location ------		description
terminal mod.	Val-7	-	C-terminal amide
uncommon	Glp-1	-	-

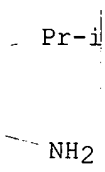
SEQ 1 XNAASFV
MF C32 H47 N9 O10
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



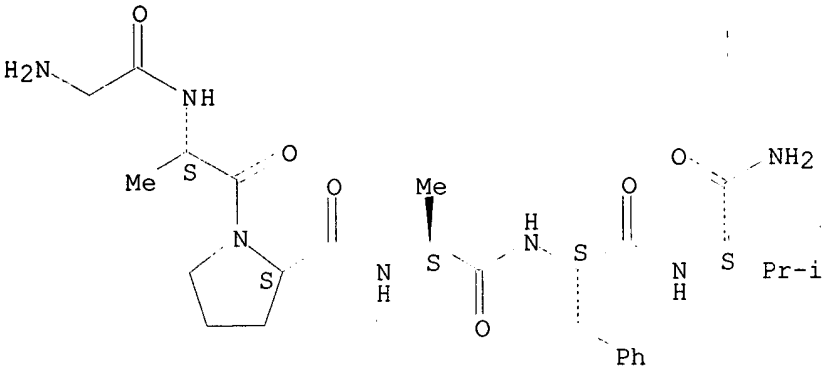
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 11 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 152247-83-1 REGISTRY Matches CAPL record #7
CN L-Valinamide, glycyl-L-alanyl-L-prolyl-L-alanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 6
NTE modified

type	------ location ------		description
terminal mod.	Val-6	-	C-terminal amide

SEQ 1 GAPAFV
MF C27 H41 N7 O6
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

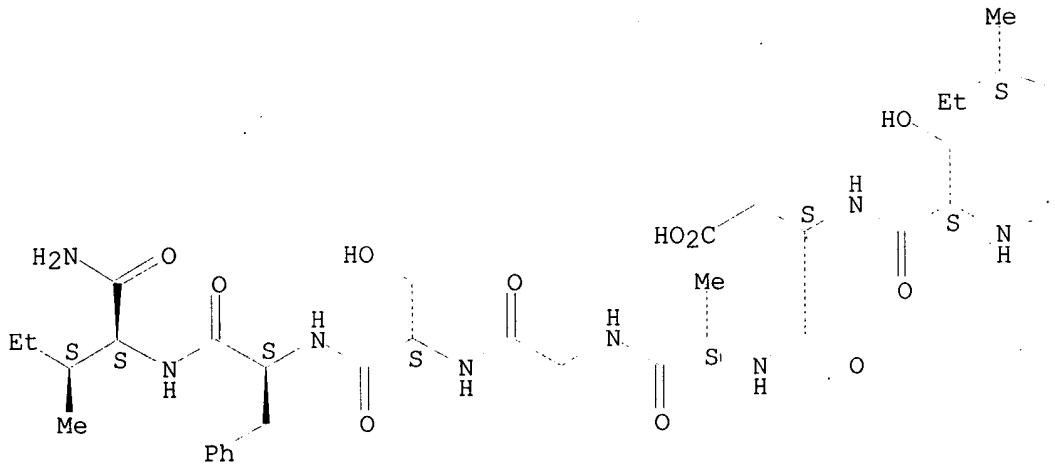
L5 ANSWER 12 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 148944-72-3 REGISTRY Matches CAPL record #9
CN L-Isoleucinamide, N2-acetyl-L-lysyl-L-isoleucyl-L-seryl-L-.alpha.-aspartyl-L-alanylglycyl-L-seryl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 9
NTE modified

type	location		description
terminal mod.	Lys-1	-	N-acetyl
terminal mod.	Ile-9	-	C-terminal amide

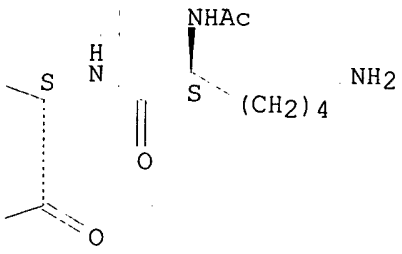
SEQ 1 KISDAGSFI
MF C44 H71 N11 O14
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 13 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 134328-61-3 REGISTRY Matches CAPL Accession #10
CN L-Leucinamide, glycyl-L-tryptophyl-L-threonyl-L-leucyl-L-asparaginyl-L-seryl-L-alanylglycyl-L-tyrosyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 10
NTE modified

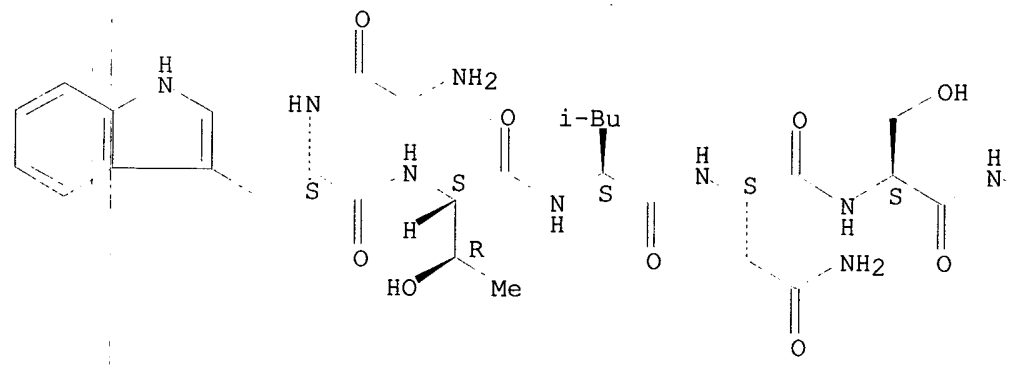
type	location		description
terminal mod.	Leu-10	-	C-terminal amide

SEQ 1 GWTLNSAGYL

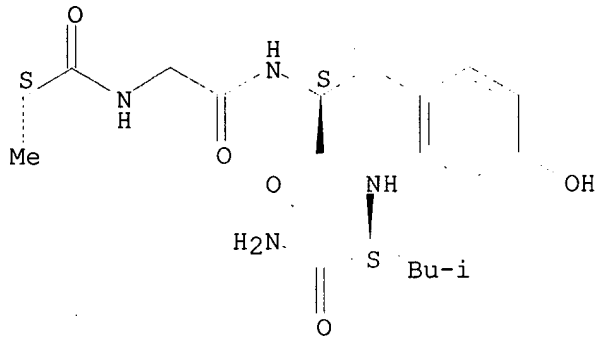
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C50 H73 N13 O14
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

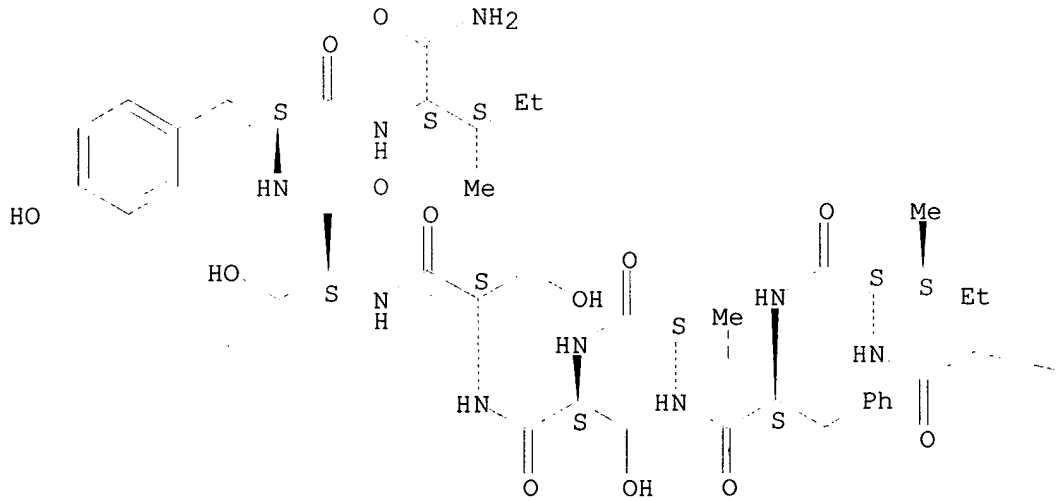
L5 ANSWER 14 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 126120-14-7 REGISTRY Matches CAPL citations 1 & 11
CN L-Isoleucinamide, glycyl-L-isoleucyl-L-phenylalanyl-L-alanyl-L-seryl-L-seryl-L-seryl-L-tyrosyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 9
NTE modified

type	location	description
terminal mod.	Ile-9 -	C-terminal amide

SEQ 1 GIFASSSYI
MF C44 H66 N10 O13
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



Searched by Barb O'Bryen, STIC 308-4291

PAGE 1-B

NH2

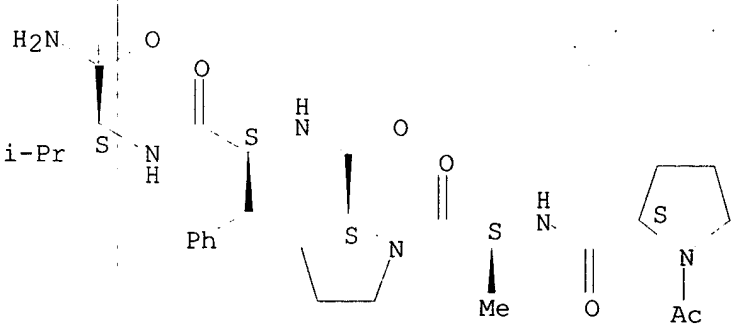
2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 15 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 100648-30-4 REGISTRY matches CAPL record #13
CN L-Valinamide, 1-acetyl-L-prolyl-L-alanyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 5
NTE modified

type	------ location ------		description
terminal mod.	Pro-1	-	N-acetyl
terminal mod.	Val-5	-	C-terminal amide

SEQ 1 PAPFV
MF C29 H42 N6 O6
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

Searched by Barb O'Bryen, STIC 308-4291

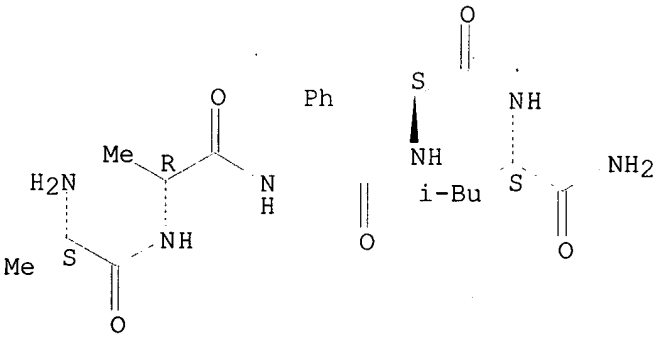
L5 ANSWER 16 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 96755-96-3 REGISTRY matches CAPL record #12 & #14
CN L-Leucinamide, L-alanyl-D-alanylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 5
NTE modified

type	------ location ------		description
terminal mod.	Leu-5	-	C-terminal amide

SEQ 1 AAGFL

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C23 H36 N6 O5
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

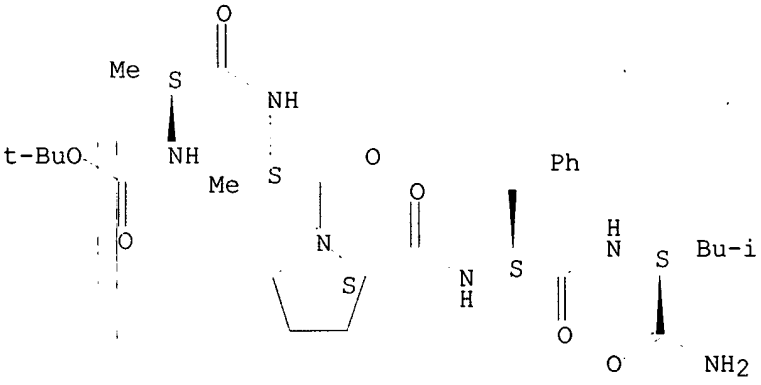
L5 ANSWER 17 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 74257-74-2 REGISTRY Matches CAPL record #15
CN L-Leucinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl-L-alanyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 5
NTE modified

type	------ location ------		description
terminal mod.	Leu-5	-	C-terminal amide
modification	Ala-1	-	(1,1-dimethylethoxy) carbonyl<Boc>

SEQ 1 AAPFL

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C31 H48 N6 O7
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

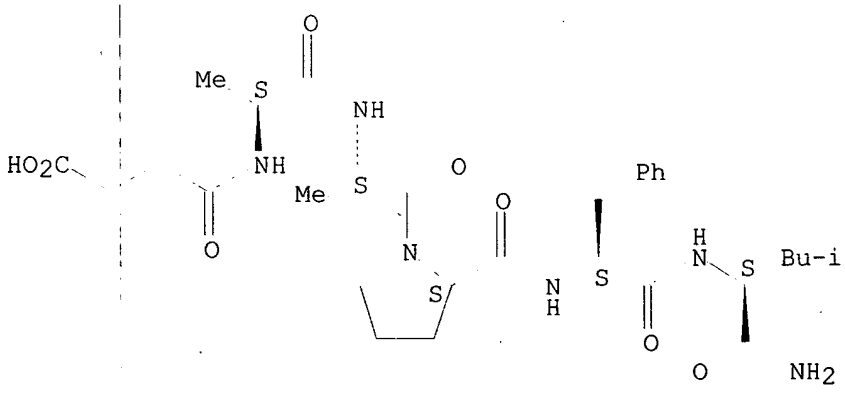
L5 ANSWER 18 OF 19 REGISTRY COPYRIGHT 2003 ACS
RN 74257-51-5 REGISTRY Matobo CAPL ans #15
CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-L-alanyl-L-alanyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 5
NTE modified

type	------ location ------		description
terminal mod.	Leu-5	-	C-terminal amide
modification	Ala-1	-	3-carboxy-1-oxopropyl<Suc>

SEQ 1 AAPFL

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C30 H44 N6 O8
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

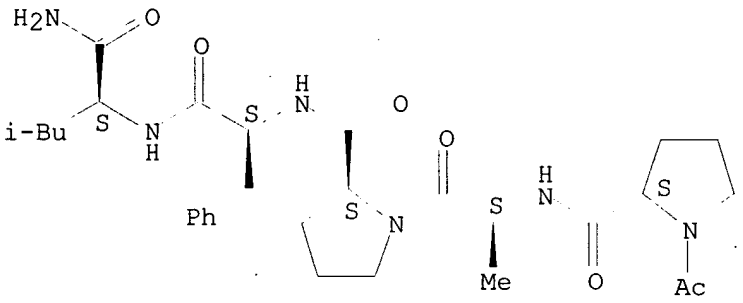
L5 ANSWER 19 OF 19 REGISTRY COPYRIGHT 2003 ACS

RN 65953-37-9 REGISTRY matches CAPL records 13 2-16
CN L-Leucinamide, 1-acetyl-L-prolyl-L-alanyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 5
NTE modified

type	location		description
terminal mod.	Pro-1	-	N-acetyl
terminal mod.	Leu-5	-	C-terminal amide

SEQ 1 PAPFL
MF C30 H44 N6 O6
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> fil capl; d que nos 16; fil uspatf; d que nos 17; dup rem 16,17
FILE 'CAPLUS' ENTERED AT 09:39:01 ON 27 JUN 2003

FILE COVERS 1907 - 27 Jun 2003 VOL 138 ISS 26
FILE LAST UPDATED: 25 Jun 2003 (20030625/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L3 STR
L5 19 SEA FILE=REGISTRY SSS FUL L3

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L6          16 SEA FILE=CAPLUS ABB=ON  L5


FILE 'USPATFULL' ENTERED AT 09:39:01 ON 27 JUN 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 26 Jun 2003 (20030626/PD)
FILE LAST UPDATED: 26 Jun 2003 (20030626/ED)
HIGHEST GRANTED PATENT NUMBER: US6584613
HIGHEST APPLICATION PUBLICATION NUMBER: US2003121088
CA INDEXING IS CURRENT THROUGH 26 Jun 2003 (20030626/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Jun 2003 (20030626/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

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>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.


L3             STR
L5          19 SEA FILE=REGISTRY SSS FUL L3
L7           1 SEA FILE=USPATFULL ABB=ON  L5



FILE 'CAPLUS' ENTERED AT 09:39:01 ON 27 JUN 2003
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FILE 'USPATFULL' ENTERED AT 09:39:01 ON 27 JUN 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L6
PROCESSING COMPLETED FOR L7
L8          16 DUP REM L6 L7 (1 DUPLICATE REMOVED)
               ANSWERS '1-16' FROM FILE CAPLUS

=> d ibib abs hitrn 1-16; fil hom

L8   ANSWER 1 OF 16  CAPLUS  COPYRIGHT 2003 ACS        DUPLICATE 1
ACCESSION NUMBER:         1994:321352  CAPLUS
DOCUMENT NUMBER:          120:321352

                          Searched by Barb O'Bryen, STIC  308-4291
```

TITLE: Method to produce immunodiagnostic reagents
INVENTOR(S): Kauvar, Lawrence M.
PATENT ASSIGNEE(S): Terrapin Technologies, Inc., USA
SOURCE: U.S., 29 pp. Cont.-in-part of U.S. 5,217,869.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5300425	A	19940405	US 1989-447009	19891206
US 5217869	A	19930608	US 1988-255906	19881011
US 5340474	A	19940823	US 1993-49642	19930409
US 5384263	A	19950124	US 1993-72190	19930604
US 5409611	A	19950425	US 1993-116059	19930902
US 5541070	A	19960730	US 1993-118133	19930908
US 5679643	A	19971021	US 1994-253433	19940531
US 5567317	A	19961022	US 1995-401445	19950309
US 5763570	A	19980609	US 1995-473397	19950607

PRIORITY APPLN. INFO.:

US 1987-108130	B2	19871013
US 1988-255906	A2	19881011
US 1988-172626	B1	19880324
US 1989-355042	A2	19890516
US 1989-429721	A2	19891031
US 1989-447009	A1	19891206
US 1990-607875	B1	19901101
US 1990-607895	B2	19901101
US 1991-678849	A2	19910402
US 1991-693245	A2	19910429
US 1992-863564	B1	19920403
US 1993-49642	A1	19930409
US 1993-116059	A3	19930902
US 1993-126229	A1	19930924

AB Screening methods to obtain suitable antibodies for use in immunoassays for analytes not ordinarily susceptible to detection by these methods involves in vitro screening of panels of cells secreting a representative selection of antibodies. An application of this method also permits the prepn. of specific mimotopes which mimic the immunol. activity of the desired analyte; the mimotopes can then be used to immunize mammals in order to improve the specificity and affinity of the antibodies. Methods to identify a particular analyte by its pattern of binding strength to a panel of related antibodies and to match an arbitrary analyte with an immunoreactive member of a panel of candidate antibodies are also disclosed. These screening methods can also be employed for rational drug design. Prepn. of a panel of antibody-secreting immortalized cells and immobilization of the panel on supported agarose are described. Nonapeptides designed to show high diversity in hydrophobic moment and hydrophoic index as well as charge distribution and size were synthesized and tested for ability to bind to 2 different monoclonal antibodies using a labeled mimotope as competitor.

IT **126120-14-7** matches Registry record #14
RL: USES (Uses)
(antibody binding ability of, immunoassay for)

L8 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:133077 CAPLUS
DOCUMENT NUMBER: 138:180761
TITLE: Methods for promoting healing of chronic dermal ulcers
INVENTOR(S): Carney, Darrell H.
PATENT ASSIGNEE(S): The Board of Regents, the University of Texas System, USA

Searched by Barb O'Bryen, STIC 308-4291

SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013569	A2	20030220	WO 2002-US1151	20020116

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-308198P P 20010727

AB Disclosed is a method of promoting healing of a chronic dermal skin ulcer, such as a diabetic ulcer, in a subject. The method comprises the step of contacting the chronic dermal skin ulcer with an effective amt. of an agonist of the non-proteolytically activated thrombin receptor.

IT **497221-38-2** matches Registry record #1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thrombin receptor agonists promoting healing of chronic dermal ulcers resulting from diabetes)

L8 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:815936 CAPLUS
DOCUMENT NUMBER: 134:69046
TITLE: Development of an antagonist of molluscan neuropeptide APGWamide with a peptide library
AUTHOR(S): Ohtani, M.; Aimoto, S.; Muneoka, Y.
CORPORATE SOURCE: Institute for Protein Research, Osaka University, Suita, 565-0871, Japan
SOURCE: Peptides (New York) (2000), 21(8), 1193-1201
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fifty-seven kinds of APGWamide-related peptides and a peptide library consisting of 38 peptide mixts., each of which contained 19 kinds of APGWamide-related peptides, were synthesized with a multipeptide synthesizer, and their APGWamide-agonistic or -antagonistic effects were examd. on the anterior byssus retractor muscle of the bivalve Mytilus edulis and the crop of the land snail Euhadra congenita. The peptide mixts. having agonistic or antagonistic effects were subjected to HPLC purifn. to isolate the active peptides using the muscles as bioassay systems. Many peptides having agonistic or antagonistic effects were obtained. Of the antagonists, APGWGNamide, isolated from the peptide mixt. of APGWGXamide, was the most potent. At 10-4 M, APGWGNamide almost completely blocked the actions of 10-6 M APGWamide on the anterior byssus retractor muscle of M. edulis and the crop of E. congenita.

IT **314057-66-4 314057-67-5 314057-69-7 314057-76-6** Matches Registry records 2, 3, 4, 5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(development of antagonist of molluscan neuropeptide APGWamide with peptide library)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:353192 CAPLUS
DOCUMENT NUMBER: 129:64726
TITLE: Product Inhibition of the Hepatitis C Virus NS3 Protease
AUTHOR(S): Steinkuehler, Christian; Biasiol, Gabriella; Brunetti, Mirko; Urbani, Andrea; Koch, Uwe; Cortese, Riccardo; Pessi, Antonello; De Francesco, Raffaele
CORPORATE SOURCE: Istituto di Ricerche di Biologia Molecolare P. Angeletti (IRBM), Rome, 00040, Italy
SOURCE: Biochemistry (1998), 37(25), 8899-8905
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The nonstructural protein NS3 of the hepatitis C virus (HCV) harbors a serine protease domain that is responsible for most of the processing events of the nonstructural region of the polyprotein. Its inhibition is presently regarded as a promising strategy for coping with the disease caused by HCV. In this work, the authors show that the NS3 protease undergoes inhibition by the N-terminal cleavage products of substrate peptides corresponding to the NS4A-NS4B, NS4B-NS5A, and NS5A-NS5B cleavage sites, whereas no inhibition is obsd. with a cleavage product of the intramol. NS3-NS4A junction. The Ki values of the hexamer inhibitory products [Ki(NS4A) = 0.6 .mu.M, Ki(NS5A) = 1.4 .mu.M, and Ki(NS4B) = 180 .mu.M] are lower than the Km values of the resp. substrate peptides [Km(NS4A-NS4B) = 10 .mu.M, Km(NS5A-NS5B) = 3.8 .mu.M, and Km(NS4B-NS5A) > 1000 .mu.M]. Mutagenesis expts. have identified Lys136 as an important determinant for product binding. The phenomenon of product inhibition can be exploited to optimize peptide inhibitors of NS3 protease activity that may be useful in drug development.
IT **208921-17-9** matches Registry record #6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(product inhibition of hepatitis C virus NS3 protease)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:633069 CAPLUS
DOCUMENT NUMBER: 127:329354
TITLE: Evidence for extensive and non-specific translocation of oligopeptides across plasma membranes of mammalian cells
AUTHOR(S): Oehlke, Johannes; Beyermann, Michael; Wiesner, Burkhard; Melzig, Mathias; Berger, Hartmut; Krause, Eberhard; Bienert, Michael
CORPORATE SOURCE: Institute of Molecular Pharmacology, Alfred-Kowalke-Strasse 4, Berlin, D-10315, Germany
SOURCE: Biochimica et Biophysica Acta (1997), 1330(1), 50-60
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB After exposure of bovine aortic endothelial cells to various small peptides (tetra- to undeca-mer), extensive transport of the peptides across the plasma membrane was obsd. in the concn. range 10-7 to 10-2 M. The obsd. transport events, which contradict the generally anticipated poor permeability of peptides across plasma membranes, exhibited high complexity and showed no saturability up to a concn. of 10-2 M. Evidence

was found for the involvement of mdrp-like transporters as well as of energy-independent facilitated diffusion events. The peptide levels within the cells approximated those of the incubation soln. within 30 min, indicating high capacity and velocity for the involved transport processes. Correspondingly, preloaded cells exported about 80% of the internalized peptide within 5 min at 37.degree.. Analogous results were found after peptide exposure to several other mammalian cell types, indicating a more general importance of the transport phenomena described here. Our findings contradict the prevailing opinion that the often obsd. lack of activity of externally administered peptides against their targets within intact cells is accounted for primarily by poor cellular uptake and point to export processes counteracting the uptake to be more important in this context.

IT **197917-26-3** matches Registry record #7
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(evidence for extensive and non-specific translocation of oligopeptides across plasma membranes of mammalian cells)

L8 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:714931 CAPLUS
DOCUMENT NUMBER: 126:42790
TITLE: Discovery of high affinity bombesin receptor subtype 3 agonists
AUTHOR(S): Wu, James M.; Nitecki, Danute E.; Biancalana, Sara; Feldman, Richard I.
CORPORATE SOURCE: Department Protein Biochemistry Biophysics, Berlex Biosciences, Richmond, CA, 94804-0099, USA
SOURCE: Molecular Pharmacology (1996), 50(5), 1355-1363
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human bombesin receptor subtype 3 (BRS-3) was cloned based on its homol. to the human gastrin-releasing peptide (GRP) receptor and neuromedin B (NMB) receptor. Some bombesin-like peptides were shown to activate BRS-3 expressed in Xenopus laevis oocytes, but only at relatively high concns., which suggests that BRS-3 is an orphan receptor. To study the pharmacol. of BRS-3 in the context of a mammalian cell, we used BR2 cells, which are Balb/3T3 fibroblasts transfected with BRS-3 cDNA. A no. of bombesin-like peptides found in mammals and amphibians stimulated calcium mobilization in BR2 cells but exhibited no effect on nontransfected parental Balb/3T3 cells. Of these peptides, NMB (EC50 .apprx. 1-10 .mu.M) was the most active for stimulation of calcium mobilization. Testing of a series of NMB analogs truncated at the amino terminus and carboxyl terminus indicated that the minimal size of NMB required for retention of full activity was Ac-NMB(3-10). Systematically replacing each residue with alanine, or changing its chirality, demonstrated that the carboxyl-terminal residues His8, Phe9, and Met10 of NMB are important for optimal activity. We also tested whether a no. of bombesin (BN) analogs that are potent pure or partial antagonists of the GRP receptor can activate BRS-3 in BR2 cells. One such analog, D-Phe6-BN(6-13) Pr amide, activated BRS-3-mediated calcium mobilization with an EC50 level of 84 nM. Through addnl. synthesis, we generated a significantly more potent analog, D-Phe6-Phe13-BN(6-13) Pr amide, which displayed an EC50 level of 5 nM for activation of BRS-3. Apparently, the core portions of bombesin-like peptides required for activation of BRS-3 are similar to those necessary for activation of the GRP and NMB receptors and thus provide pharmacol. evidence that BRS-3 is in the BN receptor family. Furthermore, we have identified an agonist of BRS-3, namely D-Phe6-Phe13-BN(6-13) Pr amide, which is roughly 1000-fold more potent than BRS-3 agonists described previously.

IT **184770-60-3** matches Registry record #8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(high-affinity bombesin receptor subtype 3 peptide agonists)

L8 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:50479 CAPLUS
DOCUMENT NUMBER: 120:50479
TITLE: Neuropeptides isolated from Helix pomatia. Part I. Peptides related to MIP, buccalin, myomodulin-CARP and SCP
AUTHOR(S): Ikeda, Tetsuya; Minakata, Hiroyuki; Fujita, Tsuyoshi; Muneoka, Yojiro; Kiss, Tibor; Hiripi, Laszlo; Nomoto, Kyosuke
CORPORATE SOURCE: Suntory Inst. Bioorg. Res., Osaka, 618, Japan
SOURCE: Pept. Chem. 1992, Proc. Jpn. Symp., 2nd (1993), Meeting Date 1992, 576-9. Editor(s): Yanaihara, Noboru. ESCOM: Leiden, Neth.
CODEN: 59NTAC
DOCUMENT TYPE: Conference
LANGUAGE: English
AB In the present study, the authors further attempted to isolate neuropeptides from H. pomatia, and characterized 63 species of peptides. Thirty-two of them were found to have a structural relation to MIPs, BUCs, myomodulin-CARP or SCPs as shown in this paper. The other 31 species are described in Part 2 of this paper.
IT **152247-83-1** matches Registry record #11
RL: BIOL (Biological study)
(of nervous system of European land snail)

L8 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:107706 CAPLUS
DOCUMENT NUMBER: 120:107706
TITLE: Elevated intrinsic reactivity of seryl hydroxyl groups within the linear peptide triads His-Xaa-Ser or Ser-Xaa-His
AUTHOR(S): Miller, Brian T.; Kurosky, Alexander
CORPORATE SOURCE: Dep. Anat. Neurosci., Univ. Texas Med. Branch, Galveston, TX, 77555, USA
SOURCE: Biochemical and Biophysical Research Communications (1993), 196(1), 461-7
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chem. modification studies of peptide hormones and random peptides have revealed that seryl hydroxyl groups had enhanced reactivity toward acylating reagents when they occurred in the linear triads His-Xaa-Ser or Ser-Xaa-His (Xaa = any amino acid). O-Acylation of Ser within these triads was achieved by reaction with N-hydroxysuccinimide esters of biotin (NHS-biotin) and succinic anhydride. Seryl residues not occurring in His-Xaa-Ser/Ser-Xaa-His triads showed no reactivity toward NHS-biotin under reaction conditions described. Results of histidine replacement studies and studies of the pH dependence of O-biotinylation indicated that the increased nucleophilicity of the seryl hydroxyl group was due to intramol. interaction between the seryl and histidyl residues. These findings provide strong evidence that such triads represent novel consensus motifs in peptides.
IT **152868-78-5 152868-80-9** matches Registry records #9 & #10
RL: RCT (Reactant); RACT (Reactant or reagent)
(attempted biotinylation of, histidine-serine triad in relation to)

L8 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:469941 CAPLUS

DOCUMENT NUMBER: 119:69941
TITLE: Microheterogeneity in the recognition of a HLA-DR2-restricted T cell epitope from a meningococcal outer membrane protein
AUTHOR(S): Wiertz, Emmanuel; Van Gaans-Van den Brink, Jacqueline; Hoogerhout, Peter; Poolman, Jan
CORPORATE SOURCE: Natl. Inst. Public Health Environ., Bilthoven, 3720 BA, Neth.
SOURCE: European Journal of Immunology (1993), 23(1), 232-9
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The trimol. interaction of T cell receptor (TcR), antigen, and major histocompatibility complex (MHC) class II was analyzed using a panel of HLA-DR2-restricted T cell clones recognizing the 49-61 region of a meningococcal class I outer membrane protein (OMP). The clones, all CD3+CD4+CD8-TcR.alpha./.beta.+, were selected by restimulation with the synthetic peptide OMP(49-61), which contains an immunodominant T helper determinant. Using a series of peptides that were sequentially truncated from the N or C terminus, 4 different epitope fine-specificity patterns were identified. Furthermore, each clone exhibited a distinct recognition pattern for a panel of 20 single-residue substitution analogs of the minimal epitope OMP(50-58). Most substitutions that were not tolerated in the nonamer were allowed when the analogs were prepd. departing from the native peptide OMP(49-61). Obviously, the residues outside the minimal epitope contribute to stabilization of the trimol. complex. Thus, defining the minimal size of T cell determinants may be of limited value. By performing proliferation competition assay, putative MHC and TcR contact residues were identified in the peptide. Most likely, isoleucine-51 and phenylalanine-54 act as MHC-anchoring residues, whereas asparagine-53 represents a crit. TcR contact residue for all of the clones. MHC anchoring may be provided by other residues as well, since isoleucine-51 and phenylalanine-54 can be substituted by conservative residues [as OMP(50-58) and OMP(49-61) analogs] and with alanine [as OMP(49-61) analogs only]. Some evidence was found for interaction of particular side chains at other positions with TcR mols., but this contribution was not equally important for all clones. Apparently, the clonotypic TcR can see a single epitope in different ways in the context of the same MHC restriction element. Since most clones use different V.alpha. and V.beta. genes (which encompass the putative MHC-binding regions 1st and 2nd complementarity-detg. regions, CDR1 and CDR2) different modes of interaction with the HLA-DR2 mol. indeed are likely to occur.

IT **148944-72-3** Metabolites Registry record #17
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of outer membrane protein, of Neisseria meningitidis, as HLA-DR2-restricted T cell epitope)

L8 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:401296 CAPLUS
DOCUMENT NUMBER: 115:1296
TITLE: Structure-activity relationships of galanin: importance of the N-terminal sequence for agonist activity on smooth muscle
AUTHOR(S): Aiken, James W.; Kaddis, Farida G. B.; Connell, Mark A.; Staples, Douglas J.; Bannow, Carol A.; Kinner, John H.; Sawyer, Tomi K.
CORPORATE SOURCE: Metab. Dis. Res. Units, Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 11th (1990), Meeting Date 1989, 205-7. Editor(s):

Searched by Barb O'Bryen, STIC 308-4291

Rivier, Jean E.; Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth.
CODEN: 56XTA7
DOCUMENT TYPE: Conference
LANGUAGE: English
GI

H-Gly-Trp-Thr-Leu-Asn-Ser-Ala-Gly-
Tyr-Leu-Leu-Gly-Pro-His-Ala-Ile-
Asp-Asn-His-Arg-Ser-Phe-His-Asp-
Lys-Tyr-Gly-Leu-Ala-NH_2 I

AB A symposium report on the structure-activity relationship of porcine galanin (GAL1-29-NH2) (I) using N-terminal sequences GAL1-12-NH2, GAL1-11-NH2, GAL1-10-NH2, GAL1-9-NH2, GAL1-8-NH2 as agonist of smooth muscle contraction.
IT **134328-61-3** Matches Registry record #13
RL: BIOL (Biological study)
(smooth muscle contraction in response to, agonist activity in)

L8 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:156551 CAPLUS
DOCUMENT NUMBER: 112:156551
TITLE: Synthetic peptides for screening of antibodies to be used in immunodiagnosis
INVENTOR(S): Kauvar, Lawrence M.
PATENT ASSIGNEE(S): Terrapin Diagnostics, Ltd., USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8903430	A1	19890420	WO 1988-US3554	19881012
W: AU, BR, DK, FI, HU, JP, KR, NO, RO, SU				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8927909	A1	19890502	AU 1989-27909	19881012
AU 635492	B2	19930325		
EP 387276	A1	19900919	EP 1988-909865	19881012
EP 387276	B1	19970423		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
HU 55143	A2	19910429	HU 1988-6713	19881012
JP 03504638	T2	19911009	JP 1988-509136	19881012
JP 07111427	B4	19951129		
AT 152244	E	19970515	AT 1988-909865	19881012
CA 1340459	A1	19990323	CA 1988-580048	19881013
JP 07072151	A2	19950317	JP 1994-32687	19940302

PRIORITY APPLN. INFO.: US 1987-108130 A 19871013
WO 1988-US3554 W 19881012

AB Screening methods to obtain suitable antibodies for use in immunoassays for analytes not ordinarily susceptible to detection by this means involve in vitro screening of panels of cells secreting a representative selection of antibodies. An application of this method also permits the prepn. of

specific mimotopes which mimic the immunol. activity of the desired analyte; the mimotopes can then be used as competitors in the immunoassay or can be used to immunize mammals in order to improve the specificity and affinity of the antibodies. Methods to identify a particular analyte by its pattern of binding strength to a panel of related antibodies and to match an arbitrary analyte with an immunoreactive member of a panel of candidate antibodies are also disclosed. A basal antibody reportoire subset was prepd. by fusing spleen cells of 10-wk-old BALB/c mice with myeloma P3X63AG8.653, culturing the cells in hypoxanthine medium, feeding with syngeneic macrophages and spleen cells, and distributing in microtiter plates to give >5000 antibody-producing cells. A panel of 88 pentapeptides (designed for decreasing hydrophobicity and periodic variation of hydrophobic moment by the method of H. Geysen (1984)) were prepd. and labeled with 125I, and a mixt. of them were tested with individual members of the basal antibody repertoire, either with or without the presence of analyte (undefined). Antibodies showing decreased binding to the peptides in the presence of analyte were analyte specific.

IT **126120-14-7P** Natoma Registry record #14
RL: ARG (Analytical reagent use); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(mimotope peptide, prepn. of, for monoclonal antibody specificity screening)

L8 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:631508 CAPLUS
DOCUMENT NUMBER: 109:231508
TITLE: The study of circular dichroism of some enkephalins, .beta.-casomorphins and dynorphins
AUTHOR(S): Kojro, Elzbieta; Gwizdala, Elwira; Grzonka, Zbigniew
CORPORATE SOURCE: Inst. Chem., Univ. Gdansk, Gdansk, 80952, Pol.
SOURCE: Polish Journal of Chemistry (1987), 61(4-6), 415-24
CODEN: PJCHDQ; ISSN: 0137-5083
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The CD spectra of compds. belonging to different series of opioid peptides, i.e. analogs of Leu-enkephalin, .beta.-casomorphin, and dynorphin, have been compared. Peptide spectra have been measured in aq. solns. at pH 2.5, 6.9, and 11.6, and in some cases in trifluoroethanol. Anal. of the CD spectra shows that Leu-enkephalins possess in soln. a rather random structure in soln., whereas the presence in .beta.-casomorphin of the sequence Pro-Gly results in the .beta.-turn type II conformation. The differences in dynorphin spectra obsd. for aq. and trifluoroethanol solns. show a preference of the helical structure in dynorphins contg. 13 or 14 amino acid residues.

IT **96755-96-3** Natoma Registry record #16
RL: RCT (Reactant); RACT (Reactant or reagent)
(CD of)

L8 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:104917 CAPLUS
DOCUMENT NUMBER: 104:104917
TITLE: Enzyme-substrate interactions in the hydrolysis of peptide substrates by thermitase, subtilisin BPN', and proteinase K
AUTHOR(S): Broemme, D.; Peters, K.; Fink, S.; Fittkau, S.
CORPORATE SOURCE: Inst. Biochem., Martin-Luther-Univ. Halle-Wittenberg, Halle/Saale, DDR-4020, Ger. Dem. Rep.
SOURCE: Archives of Biochemistry and Biophysics (1986), 244(2), 439-46
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal

Searched by Barb O'Bryen, STIC 308-4291

LANGUAGE: English
AB Peptide substrate of the general structure acetyl-Alan (n = 2-5), acetyl-Pro-Ala-Pro-Phe-Alan-NH2 (n = 0-3), and acetyl-Pro-Ala-Pro-Phe-AA-NH2 (AA = various amino acids), were synthesized and used to investigate the enzyme-substrate interactions of the microbial serine proteases thermitase, subtilisin BPN', and proteinase K on the C-terminal side of the scissile bond. The elongation of the substrate peptide chain up to the 2nd amino acid on the C-terminal side (P2') enhanced the hydrolysis rate of thermitase and subtilisin BPN', whereas for proteinase K an addnl. interaction with the 3rd amino acid (P3') was possible. The enzyme subsite S1' specificity of the proteases investigated was very similar. With respect to kcat/Km values (where kcat = catalytic const.), small amino acid residues such as alanine (Ala) and glycine were favored in this position. Bulky residues, such as phenylalanine and leucine, were hydrolyzed to a lower extent. Proline in P1' abolished the hydrolysis of the substrates. Enzyme-substrate interactions on the C-terminal side of the scissile bond appeared to affect kcat more than Km for all 3 enzymes.
IT **65953-37-9 100648-30-4** Matches Registry records 15 & 19
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with serine proteinases, kinetics of)

L8 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:406691 CAPLUS
DOCUMENT NUMBER: 103:6691
TITLE: Solid-phase syntheses of some analogs of Leu-enkephalin, .beta.-casomorphin and dynorphin
AUTHOR(S): Kojro, Elzbieta; Grzonka, Zbigniew
CORPORATE SOURCE: Inst. Chem., Univ. Gdansk, Gdansk, 80952, Pol.
SOURCE: Polish Journal of Chemistry (1984), 58(1-2-3), 163-71
CODEN: PJCHDQ; ISSN: 0137-5083
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Seventeen title peptides, e.g. enkephalin analog H-Tyr-D-Ala-Gly-Phe-Leu-NH2 (I), .beta.-casomorphin (1-5), and dynophin (1-13), were prepd. by the solid-phase method. Thus, Me3CO2C-Tyr(CH2Ph)-D-Ala-Gly-Phe-Leu-R (II, R = resin) was prepd. and then cleaved by ammonolysis to give II (R = NH2), which was deblocked by HCl/HOAc and hydrogenolysis to give I.
IT **96755-96-3P** Matches Registry record #16
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L8 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1980:545297 CAPLUS
DOCUMENT NUMBER: 93:145297
TITLE: Studies on reactivity of human leukocyte elastase, cathepsin G, and porcine pancreatic elastase toward peptides including sequences related to the reactive site of .alpha.1-protease inhibitor (.alpha.1-antitrypsin)
AUTHOR(S): McRae, Brian; Nakajima, Kiichiro; Travis, James; Powers, James C.
CORPORATE SOURCE: Sch. Chem., Georgia Inst. Technol., Atlanta, GA, 30332, USA
SOURCE: Biochemistry (1980), 19(17), 3973-8
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Most of the title peptides had a prolyl residue at the P2 site, since several serine proteases have been shown to productively bind such substrates only with the proline at the subsite (S2) adjacent to the primary substrate binding site (S1). Human leukocyte (HL) elastase prefers a valyl residue over alanine or methionine at S1, whereas porcine pancreatic (PP) elastase prefers an alanine. With both elastases,

extension of the peptide chain results in significant increases in kcat/Km. With the appropriate substrates, HL elastase is as reactive as PP elastase. Cathepsin G shows a preference for phenylalanine over methionine at S1 and a preference for phenylalanine over alanine or leucine at S1'. Extension of the peptide chain yields little increase in rate, and thus the kcat/Km values obsd. with cathepsin G are not as large as those of the other enzymes. The .alpha.1-protease inhibitor (.alpha.1-PI) reactive site has recently been shown to have the sequence -Ala-Ile-Pro-Met*-Ser-Ile-Pro-Pro-, where the asterisk indicates the bond cleaved (P1-P1') when .alpha.1-PI.cntdot.protease complexes are split. The octapeptide Ac-Ala-Ile-Pro-Met-Ser-Ile-Pro-Pro-NH2 and the analog with a P1' threonine instead of serine were synthesized. All 3 enzymes bound to and cleaved the peptides at the P1 methionine bond. The Km values were in the mM range, showing that this particular sequence alone does not account for the tight binding of serine proteases to .alpha.1-PI. The kcat values, a measure of the ease with which certain types of bond formation between proteases and .alpha.1-PI would occur, were higher for the P1' serine octapeptide than for the threonine analog, indicating that relatively minor amino acid substitutions in the .alpha.1-PI reactive site will profoundly influence its reactivity toward various proteases. Inactivation of .alpha.1-PI in the lung by oxidn. and the resulting protease imbalance is the currently accepted model for the development of emphysema. In the majority of cases studied, oxidn. of the P1 methionine residue of simple peptides to the sulfoxide resulted in decreased binding to the enzymes studied, and a decreased kcat/Km. Redn. of substrate effectiveness was greatest with HL elastase for the P1' serine peptides compared to the P1' threonine peptides. Reactive site substitution could affect the degree to which oxidn. is damaging to the inhibitor and may be 1 possible explanation for the greater susceptibility to emphysema of some individuals with normal .alpha.1-PI.

IT **74257-74-2P** matches Registry record #17
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acid cleavage and succinylation of)

IT **74257-51-5P** matches Registry record #18
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with cathepsin G)

L8 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:116975 CAPLUS
DOCUMENT NUMBER: 88:116975
TITLE: Active centers of Streptomyces griseus protease 1, Streptomyces griseus protease 3, and .alpha.-chymotrypsin: enzyme-substrate interactions
AUTHOR(S): Bauer, Carl Axel
CORPORATE SOURCE: Chem. Cent., Univ. Lund, Lund, Swed.
SOURCE: Biochemistry (1978), 17(2), 375-80
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Kinetic consts. for S. griseus protease 1 (I)-catalyzed hydrolysis of a no. of peptides of increasing chain length were detd. and indicated that the active center of the enzyme extends over 6-7 subsites (21-25 .ANG.). The rate of substrate hydrolysis was highly dependent on the peptide chain length, the rate increase being .gtoreq.107-fold on going from a specific acetylamino acid amide to an acetylheptapeptide amide. This rate increase was largely due to an increase in the acylation rate. The specificity of the S1 and S1' subsites of I was investigated with peptide substrates. Addnl. data on the specificity of these subsites in S. griseus protease 3 and chymotrypsin were also presented. Generally, the specificities of the S1 subsites in the 3 enzymes were similar. However, there were important differences between the microbial and the pancreatic enzymes' ability to hydrolyze peptides with certain P1 residues, notably tryptophan. The

implications of the kinetic data for the structures of the S1 subsites were discussed. Exchanging the P1' amino group of a tetrapeptide for a P1' amino acid amide increased the hydrolysis rate in all 3 enzymes, the increase being as large as 100-fold in the most favorable case. The abilities of the enzymes to use strain in facilitating hydrolysis of the P1' residue differed markedly. Available kinetic and crystallog. data were used to throw light on the role of the active center structure for the rate of peptide substrate hydrolysis in the above 3 enzymes and trypsin, elastase, and subtilisin BPN'.

IT **65953-37-9** matches Registry record # 19
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of, kinetics of enzymic)

FILE 'HOME' ENTERED AT 09:39:17 ON 27 JUN 2003

STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 97527

TO: Regina DeBerry **Location: CM1/10D08/10B19** **Art Unit: 1647** **Friday, June 27, 2003** **Case Serial Number: 909122**	**From: Barb O'Bryen** **Location: Biotech-Chem Library** **CM1-6A05** **Phone: 308-4291** **barbara.obryen@uspto.gov**

Search Notes

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

Mary Hale, Information Branch Supervisor
308-4258, CM1-1E01

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library CM1 – Circ. Desk

Sequence Family Search of Proteins (/sqsfp)

In the sequence family search, each amino acid in the query has to match either the exact amino acid or a family member equivalent, as shown in the Family Equivalence Table below. The Family Equivalence Table is applied only to each common amino acid in the sequence. Specific uncommon amino acids may be included in the sequence; however, family equivalents only exist for the common amino acids. An amino acid family is based on a conservative substitution of amino acids sharing a similar chemical property. Each common amino acid in the query is converted to its family class members in a search. A match occurs on a query sequence if each amino acid is exactly matched or any of its family members are encountered. For example, the Hydrophobic-Aromatic family consists of the common amino acids F, W, and Y. If the amino acid F is specified within a sequence exact family search, it will match on amino acids F, W, or Y.

FAMILY EQUIVALENCE TABLE

Family Class Name	Family Class Members
Neutral-Weakly Hydrophobic	Ala (A), Gly (G), Pro (P), Ser (S), Thr (T)
Hydrophilic-Acid Amine	Asn (N), Asp (D), Gln (Q), Glu (E)
Hydrophilic-Basic	Arg (R), His (H), Lys (K)
Hydrophobic	Ile (I), Met (M), Leu (L), Val (V)
Hydrophobic-Aromatic	Phe (F), Trp (W), Tyr (Y)
Crosslinking	Cys (C)

Ex. DeBerry -

CAS considers amino acids within the same "family class" to have similar chemical properties. Within the same "family class", the members are allowable conservative substitutions for each other.

I broadened your search request to allow for this conservative substitution.

Seq 6 = A G T K P D E G K R G D A C E G D S [redacted]

P P G W L
A A A Y M
S S S I
T T T

I searched the highlighted portion, allowing for the conservative substitutions listed below each AA.

Rob